DNA dominos on a chip

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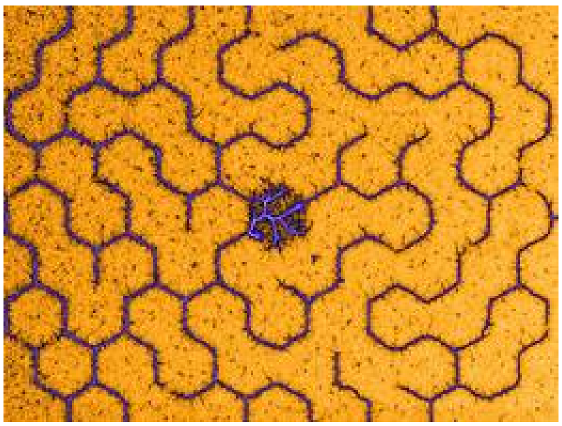

Labyrinth of condensed DNA molecules. Credit: G. Pardatscher / TUM

Normally, individual molecules of genetic material repel each other. However, when space is limited DNA molecules must be packed together more tightly. This case arises in sperm, cell nuclei and the protein shells of viruses. An international team of physicists has now succeeded in artificially recreating this so-called DNA condensation on a biochip.

Recreating important biological processes in cells to better understand them currently is a major topic of research. Now, physicists at TU Munich and the Weizmann Institute in Rehovot have for the first time managed to carry out controlled, so-called DNA condensation on a biochip. This process comes into play whenever DNA molecules are closely packed into tight spaces, for example in circumstances that limit the available volume.

This situation arises in cell nuclei and in the protein shells of viruses, as well as in the heads of sperm cells. The phenomenon is also interesting from a physical perspective because it represents a phase transition, of sorts. DNA double helices, which normally repel each other because of their negative charges, are then packed together tightly. "In this condensed state they take on a nearly crystalline structure," says co-author and TU professor Friedrich Simmel.

Nano hairs

The international team led by Simmel and his Israeli colleague Roy Bar-Ziv managed to bond DNA molecules only one thousandth of a millimeter long (i.e. several thousand base pairs long each) tightly to nanostructures of varying widths on a chip. The result looks as though the researchers had planted tiny hairs onto the chip surface.

Due to their negative charge, DNA molecules repel each other, giving the appearance of tiny nanohairs standing on end. The process of condensation was initiated when the researchers added an agent called spermidine, whose molecules have multiple positive charges. The previously upright DNA threads collapsed one after the other, dropping systematically onto the fine structures of the next thread.

This is like a domino cascade at the nanoscale. The result was compact layers of DNA molecules, packed as densely as they are in cell nuclei. All DNA molecules fell along the predefined path. "This is a very dramatic process," says Simmel. "The DNA is instantly bundled in a single direction."

Condensation and decondensation, i.e. the renewed unpacking of DNA strands, play an important role in processes like gene expression. When the DNA molecules are densely packed, for example, the information coded in them cannot be read.

New insight from the DNA chip

The researchers thus have a further building block for creating artificial cells on the surface of chips and studying all associated phenomena. "It is quite plausible to implement cell-like systems with densely packed DNA on a chip," says Simmel. DNA condensation could then be used to improve the control of gene expression and copying of genetic information in these kinds of artificial cells.

In principle, it is also possible to use the densely packed DNA molecules to relay and distribute signals and information via a kind of conducting path on such biochips. Condensation and decondensation could be used as on/off switches with good temporal control.

Friedrich Simmel would not be a passionate researcher if he did not, in addition to technical application perspectives, have his eye on basic physics. "We also want to understand the conditions of the phase transition during condensation," says Simmel. "For this we have ideal conditions on the chip. We can precisely control where the condensation occurs and how long it takes."

This is somewhat like supercooled water or beer in the freezer box, in which the liquid freezes abruptly starting at a specific point with a crystallization seed and then spreads outwards from there. The only difference is that the phase transition is not controlled by temperature, but rather the concentration of positively charged molecules. The research was funded by the Volkswagen Foundation, the German Research Foundation via the Excellence Cluster Nanosystems Initiative Munich (NIM), the Israel Science Foundation and the Minerva 80 Foundation.

More information: Günther Pardatscher et al, DNA condensation in one dimension, *Nature Nanotechnology* (2016). DOI: 10.1038/nnano.2016.142

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